Chapter 6:

In situ control of polymer helicity with a non-covalently bound motor.

In this chapter the transfer of chirality from a molecular motor to a dynamic helical polymer via ionic interactions was investigated. A molecular motor acting as a dopant with photoswitchable chirality was able to induce a preferred helicity in a poly(phenylacetylene) polymer and the helicity is inverted upon irradiation.

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6.1 Introduction

Dynamic helical polymers, such as poly(phenylacetylene)s, poly(quinoxaline-2,3-diyl)s and poly(isocyanates) (Figure 1) are macromolecules with intriguing properties and functions.[1] Prominent examples of applications include the use of these polymers as tunable chiral column material,[2] polymeric catalysts[3] or as sensing materials for the detection of very small ee's.[4] Moreover, many responsive and smart materials are based on these polymers.[5]

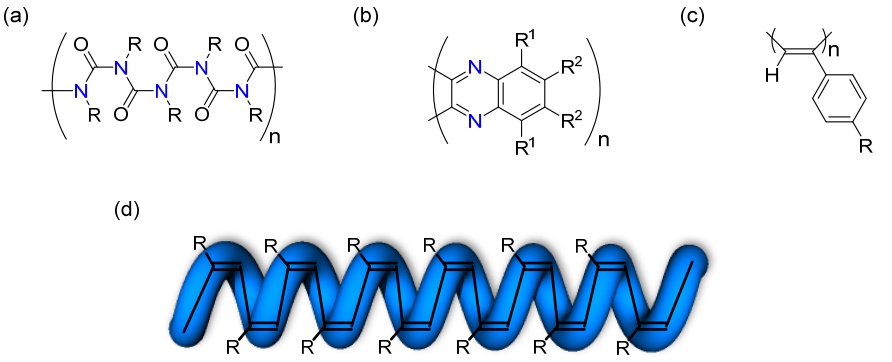


Figure 1. (a) Poly(isocyanate). (b) Poly(quinoxaline-2,3-diyl). (c) Poly(phenylacetylene). (d) Representation of the helical conformation of poly(phenylacetylene).

Poly(phenylacetylene)s have several conformational and configurational isomers. In the case of *trans* configured double bonds, the poly(phenylacetylene) is achiral, while the *cis* isomer of the polymer has a helical conformation. The dihedral around the single bond of the main chain determines the pitch of this helix. The *cis-cisoid* isomer gives a contracted helical structure, while the *cis-transoid* conformation gives rise to a more elongated helical form. The catalyst for the polymerization of phenylacetylenes dictates the configuration of the double bond. Conditions such as temperature, solvent or pH determine whether the single bond adopts a more *cisoid* or *transoid* conformation.[1e]

The helical structure of poly(isocyanate)s, poly(quinoxaline-2,3-diyl) and poly(phenylacetylene)s consists of domains of either *P* or *M* handedness which are in equilibrium with each other via a low inversion barrier, hence the name dynamic helical polymers. Without any source of external chirality, the overall composition is racemic. The introduction of chirality, either by chiral appendages or via non-covalent binding leads to one preferred handedness of the polymer.

Control over the polymer helicity by light could be a promising approach towards the design of photoaddressable systems of which the property and function can be modulated. Examples of inversion of helical chirality with light are however, limited. For polyisocyanates functionalized with either azobenzenes,[6] bicyclic ketones[7] or

molecular motors[8] inversion of helicity could be accomplished using light (Figure 2). In the first two examples, the photoswitches were incorporated as side chains In the latter case the motor is used as the initiator in the polymerization. In this way a polyisocyanate is obtained with a single molecular motor at the end. It was found that this single moiety is able to induce a preferred helicity in the polymer. Moreover, the photoisomerization of the motor resulted in the overall reversal of the handedness of the polyisocyanate chain. This example showcases how the transfer of chirality[9] can be used to dictate the structure of dynamic helical polymers, and opens up the possibility to control the function of these polymers via molecular motors.

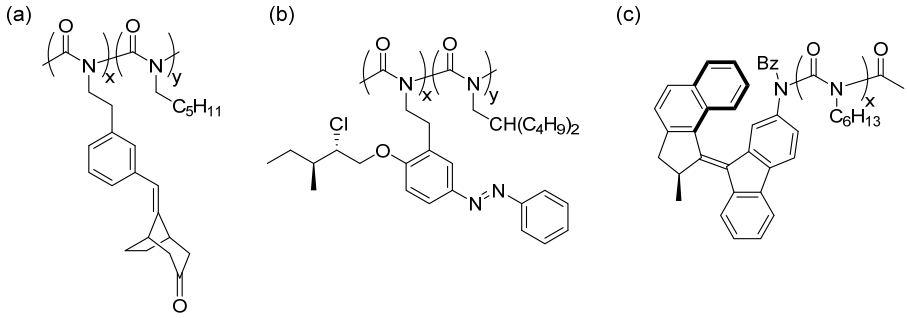


Figure 2: (a) Poly(isocyanate) functionalized with a axially chiral ketone. Irradiation of this moiety with circularly polarized light leads to photoresolution. (b) poly(isocyanate) with azobenzene moieties. (c) poly(isocyanate) polymer functionalized with a single motor.

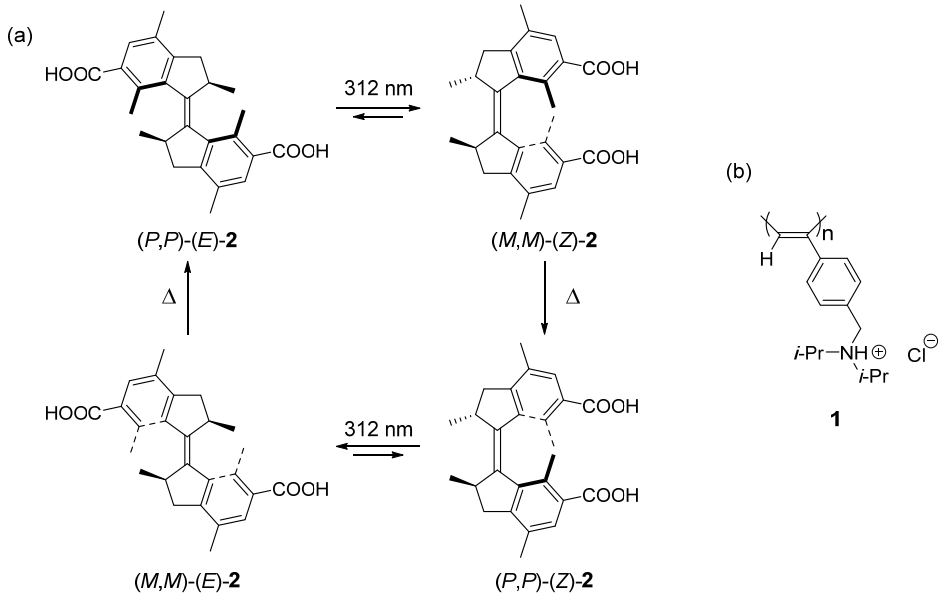
Inspired by the great potential of dynamic helical polymers in combination with molecular motors, it was anticipated that alternative ways of transfer of chirality could be more beneficial. Although the covalent functionalization of dynamic helical polymers with molecular motors has been a successful strategy towards developing photoresponsive dynamic helical polymers, strategies that are based on less synthetic effort and which feature a higher degree of reversibility, can offer attractive alternatives. The non-covalent binding of molecular motors with dynamic helical polymers could offer a versatile and viable approach, as it allows for facile screening of various photoswitchable dopants, which can be detached by a chemical stimulus. The non-covalent binding of photoresponsive dopants to dynamic helical polymers has to the best of the author's knowledge, not been explored yet. Towards this goal, especially the poly(phenylacetylene) polymers are highly suitable, as it has been shown in an overwhelming number of cases that the non-covalent binding of dopants leads to one preferred helical form.[1a,b]

6.2 Results and Discussion

The water-soluble polymer developed by Yashima and co-workers, a poly(phenylacetylene) with ammonium side groups (Scheme 1b) offers a good starting

point for its ability to bind hydrophobic molecules (e.g. BINOL).[10] In our design of a photoresponsive dopant, it was reasoned that, next to the hydrophobic interactions, ionic interactions could add to the binding strength. For this reason, it was opted to investigate the interaction of dicarboxylic acid functionalized motor **2** with polymer **1** (Scheme 1). For the synthesis of **1** the procedure developed by Yashima and co-workers was followed.[10] The synthesis of (*R*,*R*)-**2** was performed by Depeng Zhao according to a previously reported procedure.[11]

The four different diastereoisomers of **2**, i.e. (*P*,*P*)-(*E*)-**2**, (*M*,*M*)-(*E*)-**2**, (*P*,*P*)-(*Z*)-**2** and (*M*,*M*)-(*Z*)-**2**, can be interconverted into each other using light and heat as stimuli, as was concluded from ^{1}H NMR and CD spectroscopy studies. (Scheme 1). At room temperature, however, only three states of **2** are accessible due to the small half-life ($t_{1/2}$ < 1 min) of (*M*,*M*)-(*E*)-**2**. Hence, **2** functions effectively as a three-state chiral switch. Irradiation of either (*P*,*P*)-(*Z*)-**2** or (*P*,*P*)-(*E*)-**2** with 312 nm light at rt gives the same photostationary state (PSS) mixture of (*P*,*P*)-(*E*)-**2** and (*M*,*M*)-(*Z*)-**2** (35:65). The other metastable isomer (*M*,*M*)-(*Z*)-**2** has a considerable higher thermal stability. The reaction rate of the THI of this isomer was determined by UV/Vis spectroscopy at five temperatures between 50 °C and 70 °C in H_2O. The Gibbs free energy of this process was determined by Eyring plot analysis and was found to be 100 kJ mol^{-1} corresponding to a half-life of approximately 21 h at 20 °C.



Scheme 1 (a) Photochemical and thermal isomerization steps of a molecular motor **2** (b) Water-soluble dynamic helical polymer developed by Yashima et al.[10]

Next, the chirality transfer of **2** to **1** was studied. The doping was accomplished by the slow evaporation of a solution of (*P*,*P*)-(*Z*)-**2** or (*P*,*P*)-(*E*)-**2** in Et_2O layered on top of a solution of **1** in double distilled H_2O (1 mg mL^{-1}). Filtration gave a clear solution which was analyzed by CD spectroscopy. The obtained CD spectra were comparable to those of **1** doped with either BINOL or chiral carboxylic acids (Figure 3),[10,12] confirming that **2** interacts with **1** and is able to induce a preferred helicity in the polymer backbone. Interestingly, the CD spectrum of **1** doped with (*P*,*P*)-(*E*)-**2** is the mirror image of the CD spectrum of **1** doped with (*P*,*P*)-(*Z*)-**2**, even though the *E* and *Z* isomers have the same absolute configuration at their stereogenic centers and the same helical chirality in their core.

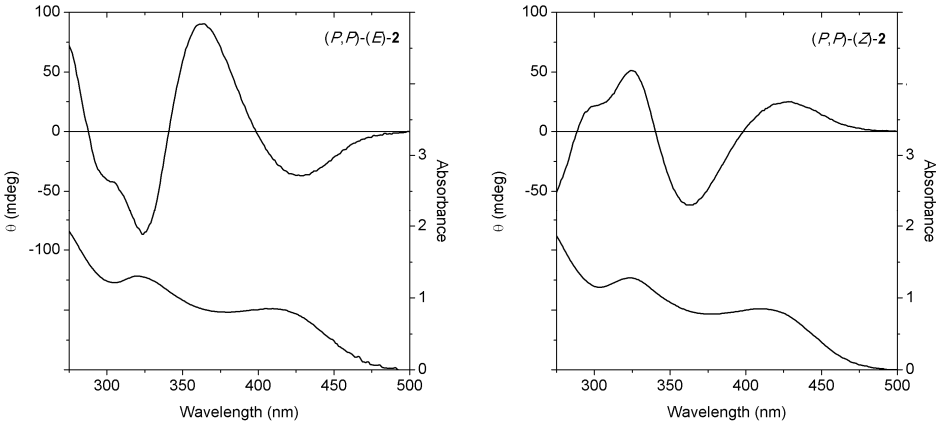


Figure 3: CD and UV/vis absorption spectrum of a solution of **1** in H_2O (1 mg mL^{-1}) doped with (*P*,*P*)-(*E*)-**2** (Left) and (*P*,*P*)-(*Z*)-**2** (Right).

Considering the structural differences between (*P*,*P*)-(*E*)-**2** and (*P*,*P*)-(*Z*)-**2**, most notably the distance between the carboxylic acid groups (approximately 11 Å and 6 Å, respectively), it is proposed that their binding modes are distinct, leading to a different preferred polymer handedness. Based on modelling of similar polymers,[13] it is estimated that the length of 6 Å and 11 Å corresponds roughly to the distance between three and five repeating units, respectively.

By varying the amount of dopant added, it was found for both (*P*,*P*)-(*E*)-**2** and (*P*,*P*)-(*Z*)-**2** that the CD signal of **1** did not increase further when more than 0.04 mg of dopant was used per 1 mg of polymer. In other words, the polymer was saturated at a molar ratio of about 0.025:1 (dopant : monomer unit), which represents an efficient transfer of chirality from the dopant to the polymer. This result is also in accordance with the findings of Yashima et al., showing an efficient transfer of chirality from BINOL to **1** in H_2O.[10]

The effect of pH and salt addition was investigated in order to get more insight in the specific mode of binding of **2** to **1**. The concentration of NaCl was increased from 0 M

to 1 M, which led to a decrease in the amplitude of the CD signal of more than a factor of two, while the UV/vis spectrum remained unchanged (Figure 4). It is expected that the addition of NaCl results in a decrease in the strength of the ionic interactions between the ammonium groups of **1** and the carboxylate groups of **2**.

Decreasing the pH to 1, at which the carboxylate groups are in their neutral carboxylic acid form, resulted in the disappearance of the CD signal. The signal reappeared when the pH of the same sample was increased back to 7, albeit of lower intensity (Figure 5). Furthermore, in a control experiment it was found that the corresponding methyl ester of **2** did not induce any CD signal. From these combined observations, it can be concluded that the ionic interactions between the carboxylate and ammonium moieties are crucial for the transfer of chirality from **2** to **1**.

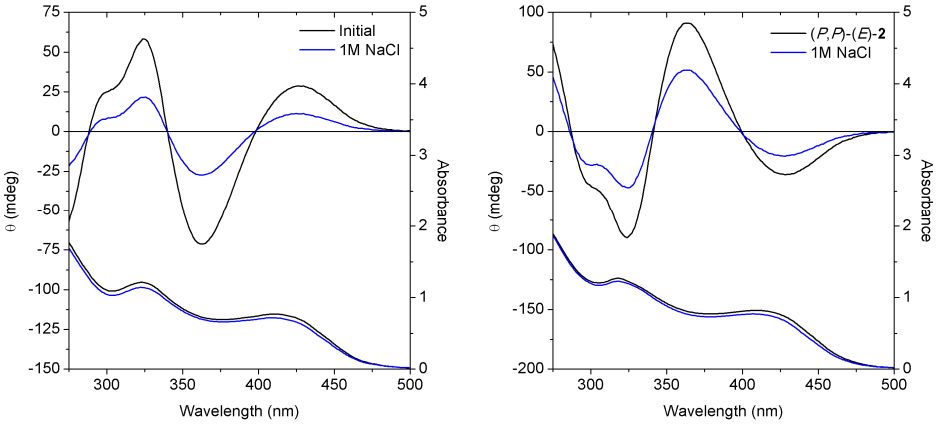


Figure 4: Effect of the addition of NaCl on the CD absorption spectrum of a solution of **1** (1.0 mg/mL) doped with (*P*,*P*)-(*Z*)-**2** (Left) and (*P*,*P*)-(*E*)-**2** (Right).

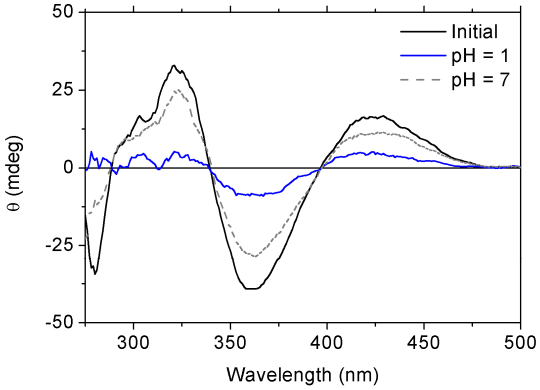


Figure 5: CD spectra of a solution of **1** (0.5 mg/mL) doped with (*P*,*P*)-(*Z*)-**2** at different pH values.

After establishing that **2** binds to **1**, it was investigated whether **2** could still be photoisomerized while associated to the polymer and how this would influence the helical conformation. Irradiation at 312 nm of a sample of **1** doped with (*P*,*P*)-(*Z*)-**2** resulted in an inversion of the CD signal and hence, the inversion of the handedness of the polymer (Figure 6). Irradiation of (*P*,*P*)-(*Z*)-**2** at room temperature gives a PSS mixture of (*M*,*M*)-(*Z*)-**2** and (*P*,*P*)-(*E*)-**2**. As indicated above, (*P*,*P*)-(*E*)-**2** induces the opposite helicity in **1**, compared to (*P*,*P*)-(*Z*)-**2**. It is proposed that (*M*,*M*)-(*Z*)-**2**, as it is a pseudo-enantiomer of (*P*,*P*)-(*Z*)-**2**, induces the opposite helicity (compared to (*P*,*P*)-(*Z*)-**2**). It must be noted that when an irradiated sample was left over time, both its CD as UV absorptivity decreased, indicating degradation of the polymer due to the exposure to UV light. Interestingly, it was found that the addition of NaCl (1 M) decreases the irradiation time required to reach the PSS. This observation indicates that the dopant first needs to dissociate in order to photoisomerize after which it can associate again and induce the opposite helicity. In sharp contrast, when a sample of **1** doped with (*P*,*P*)-(*E*)-**2** was irradiated, no inversion of the CD signal was observed, only a decrease in intensity in the CD spectrum (Figure 6). This is expected as the irradiation of (*P*,*P*)-(*E*)-**2** at room temperature give rise to a mixture of (*M*,*M*)-(*Z*)-**2** and (*P*,*P*)-(*E*)-**2**, which as reasoned above, would both induce the same helicity in **1**. The decrease in CD signal could be attributed to a somewhat lower inducing effect of (*M*,*M*)-(*Z*)-**2** compared to (*P*,*P*)-(*E*)-**2**. The photoisomerization of (*P*,*P*)-(*E*)-**2** to PSS would therefore result in a small decrease, but not in an inversion of the CD signal of **1**.

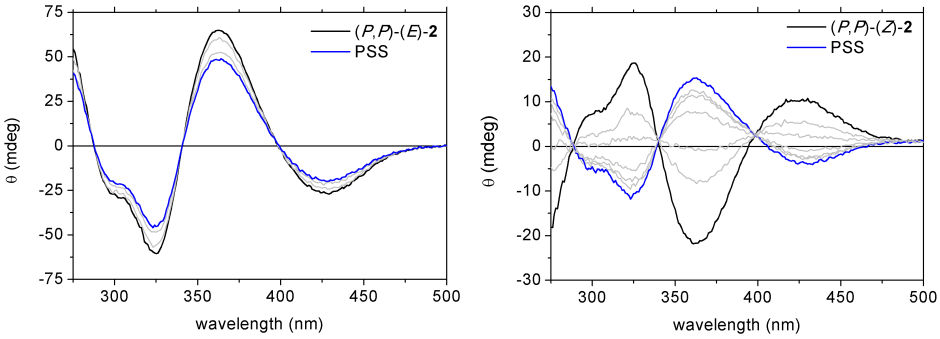


Figure 6: Changes in CD absorption spectrum of **1** in H_2O (1 M NaCl) doped with (*P*,*P*)-(*E*)-**2** upon irradiation at 312 nm. (Left) Changes in CD absorption spectrum of **1** in H_2O (1 M NaCl) doped with (*P*,*P*)-(*Z*)-**2** upon irradiation at 312 nm (Right).

6.3 Conclusions

In conclusion, it is shown that the photoswitchable chirality of a dopant can be transferred to dynamic helical polymers via non-covalent interactions. Moreover, the helicity could be inverted in situ using light as stimulus. These results pave the way for the development of functional supramolecular assemblies using the combined strength

of functional dynamic helical polymers and chiral overcrowded alkenes. Further research focuses on the development of dynamic helical polymers of which, for example, the templating abilities or the catalytic properties can be controlled via non-covalently bound molecular motors.

6.4 Experimental Section

General Remarks

Compounds **1** (M_n: 2.6 x 10^5, M_w/M_n: 3.2)[10] and **2**[11] were synthesized following procedures described in the literature. CD spectroscopy was performed on a Jasco J-715 or J-810 Spectropolarimeter in a 1 mm quartz cuvette. H_2O was distilled twice prior to use. Irradiation experiments were performed using a Spectroline model ENB-280C/FE lamp (λ_{max} = 312 nm). The doping of **1** was performed in the following way: 1 mL of a solution of **2** in Et_2O (0.1 mg mL^{-1}) was layered on top of a 1 mL solution of **1** (1 mg mL^{-1}) in H_2O. The biphasic system was stirred overnight to allow complete evaporation of the ether layer. The resulting suspension was filtered over a syringe filter and collected in a 1 mm cuvette.

6.5 References

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